

Surgical Research Society Abstracts

Br. J. Surg. 1990, Vol. 77, June,
691-713

The following abstracts are from the papers presented at the 71st meeting of The Surgical Research Society, held at the University of Liverpool, on 11-12 January 1990.

Effects of Sandostatin in ameliorating the complications of small bowel obstruction in rats

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Mechanical bowel obstruction results in distension, strangulation, vascular compromise and necrosis of the intestine. Since Sandostatin (SMS) stimulates water and electrolyte absorption and inhibits water secretion in the small bowel, we have studied its effects on intestinal secretory disturbances in rats with complete small bowel obstruction.

Six hours after construction of a 10 cm closed loop of terminal ileum, male Wistar rats were randomized to receive SMS (2 µg SC) or saline. The dosing regimen was repeated every 12 h. Twenty-four and 48 h after the start of the treatment, ileal blood flow was determined in 12 animals in each group. The rats were killed, the closed loops removed, the volume of the luminal contents measured and analysed for electrolytes, the loops weighed and a portion examined histologically.

The closed loops of SMS-treated animals appeared normal macroscopically and microscopically whereas those of control animals were grossly distended with microscopic features of inflammation and necrosis. The weight of the SMS loops (0.891 ± 0.05 g at 24 h; 1.12 ± 0.072 at 48 h) were significantly less ($P < 0.001$, Student's *t* test) than control animals (1.54 ± 0.11 g at 24 h; 2.05 ± 0.05 g at 48 h) but the dry weights did not differ significantly. The volume and electrolyte output of the loops in the SMS group were significantly less than in controls at 24 and 48 h. Blood flow to the closed loop (in $\text{mg min}^{-1} \text{g}^{-1}$ dry tissue) was significantly greater ($P < 0.001$) in SMS-treated animals (4.6 ± 0.3 at 24 h; 4.3 ± 0.4 at 48 h) than in control animals (1.7 ± 0.4 at 24 h; 0.9 ± 0.9 at 48 h).

The results of this study suggest that SMS may be a useful adjuvant treatment to surgery in small bowel obstruction, particularly in patients with recurrent partial obstruction postoperatively.

Antitropic effect of dietary calcium in subjects at increased risk for colon cancer

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Cell proliferation is increased in the large bowel of subjects at high risk of colon cancer. This abnormality has been proposed as a biomarker of cancer risk in the analysis of nutritional intervention in both human and animal models¹. It has been postulated that increased dietary calcium may be protective against colon cancer.

We have studied dietary supplementation with calcium in nine subjects with colonic polyps. Rectal biopsies before and at the end of 14 days calcium (1200 mg/day) were assessed for changes in crypt cell production rate (CCPR) and bromodeoxyuridine (BRDU) labelling. In addition, putative mechanisms for the protective effect of calcium were analysed in stool collections performed before and at the end of the study period.

Mucosal proliferation decreased on oral calcium with a fall in CCPR ($11.4-8$ cells $\text{crypt}^{-1} \text{h}^{-1}$, $t = 3.3$, $P < 0.05$) and a significant downward shift in the distribution of BRDU labelling within the colonic crypts. Stool analysis revealed significant increases in free faecal water (median: pre 29.6%; post 45.0%; $P = 0.03$) and calcium concentration (median: pre 178 mmol/kg; post 270 mmol/kg, $P = 0.008$), a trend to decreased total bile acid concentration ($5.1-4.0$ mmol/kg, $P = 0.08$) and a reduction in the ratio of lithocholic to deoxycholic acid (82-68, $P = 0.007$).

Calcium reduces the abnormal proliferation in the at-risk colon. This effect is mediated by an altered faecal bile acid profile and a possible diluent effect on toxins present in the faecal stream.

1. Lipkin M. Biomarkers of increased susceptibility to gastrointestinal cancer: new application to studies of cancer prevention in human subjects. *Cancer Res* 1988; 48: 235-45.

Effect of OKT3 on natural killer activity

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Natural killer (NK) cells may play a role in the immunosurveillance of malignant cells. They may also be precursors of lymphokine activated killer (LAK) cells which have an antitumour effect *in vivo*, although the mode of activation is unclear. The monoclonal antibody to the CD3 antigen (OKT3) has a mitogenic effect *in vitro*, leading to T-cell activation with LAK-cell proliferation. We have studied NK function *in vitro* after OKT3 pretreatment of peripheral blood lymphocytes (PBL) from normal healthy individuals. PBL, isolated by Ficoll-Hypaque centrifugation, were assessed for NK activity in a 4 h chromium-51 release assay using K562 as targets. PBL were pretreated for 30 min at 37 °C with OKT3 (1.1-0.11 µg/ml) before addition of target cells. Results are expressed as lytic units, where one lytic unit (LU) is the number of effectors required for 30 per cent cytotoxicity).

	NK activity ($10^{-3} \times \text{LU}/10^4$ PBL) in individual No.							
	1	2	3	4	5	6	7	8
Control	63	49	10	52	50	116	13	1
OKT3	163	115	57	94	79	119	54	15
Increase (%)	159	135	470	81	58	63	315	1400

OKT3 at 0.11 µg/ml: $P < 0.001$ for each individual

OKT3 pretreatment of fresh PBL consistently enhanced NK activity in all individuals (median = 147 per cent; range 58-1400) at all OKT4 concentrations tested. These results may be due to a soluble mediator(s) produced by CD3-positive cells in enhancing the activity of CD-positive NK cells and the role of cytokine involvement is under further investigation.

Selective uptake of glutamine in the gut: confirmation in a human study

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Recent animal data suggest that the gut may play a far more important metabolic role than previously thought¹. During critical illness disruption in bowel-barrier function may result in a chronic hypermetabolic state and contribute to multiorgan failure. Animal studies have demonstrated that the enterocytes of the gastrointestinal tract use glutamine (Gln) as a respiratory fuel and during critical illness the consumption of Gln by the gut significantly increases. The selective uptake of Gln by the gut has not, to date, been confirmed in humans. Seven patients who sustained multisystem trauma necessitating laparotomy underwent portal venous catheterization. This was done by reopening the umbilical vein, facilitating access to the left branch of the portal vein using a standard central venous catheter. Portal venous and systemic blood samples were recorded for five days postoperatively. Amino acid levels in both circulations were recorded at 48 h and 5 days. The percentage differences between individual amino acids in portal and systemic circulations were compared. Student's *t* test for related samples was used to determine statistical significance. At 48 h, portal venous Gln was 84 ± 5 per cent (s.d.) lower than systemic levels ($P < 0.002$). At 5 days, portal Gln was 87 ± 3 per cent lower than systemic serum ($P < 0.003$). This study confirms, for the first time in humans, that selective uptake of Gln occurs in the gut. In stressed states, Gln deficiency is associated with gut mucosal atrophy. This has significant implications as Gln is not provided in current parenteral nutrition formulations.

1. Wilmore DW, Smith RJ, O'Dwyer ST *et al*. The gut: a central organ after surgical stress. *Surgery* 1988; 104: 917-23.